



NATIONAL RESEARCH COUNCIL  
CANADA

ATOMIC ENERGY PROJECT

CHALK RIVER, ONT.

November 2nd, 1948.

Dr. Joshua Lederberg,  
Department of Genetics,  
The University of Wisconsin,  
Madison 6, Wisconsin.

Dear Joshua,

Thank you for your letter and for the extremely interesting information concerning the diploid Kl2 and its possible use for determining the delay between segregation and phenotypic expression.

I should like very much to see the experiment done, particularly as the delay appears to be absent in the case of mutation to streptomycin resistance. Thus, the magnitude of the delay is apparently a function of the particular mutation, and from a comparison of various delays one might gain some idea of the degree of permanence of the systems or structures altered by the mutation.

As streptomycin resistance is an easy character to work with, I would suggest that it be added along with  $V_1^r$  and  $V_{1a}^r$ . (Streptomycin resistant mutants will grow in any concentration of streptomycin up to and including 4000 units per cc; 32 units per cc. is adequate to inhibit the growth of all susceptible bacteria. The simple resistant and resistant-dependent (sr and sd) forms arise at very similar mutation rates, approximately  $10^{-10}$ , and are selected by plating large populations with liquid agar containing 64 or 128 units per cc.) I can put this character on any of your haploid strains, here, if you like.

I am not quite clear as to the degree of accuracy with which one can compare the rising proportions of resistant segregants with the declining proportions of heterozygous diploids. in a culture; or whether the diploids are mono- or polynucleate. In the latter case I assume that individuals containing a mixture of diploid and haploid nuclei, or more than one type of haploid nucleus, would give rise to mosaic or sectorial colonies on EMB agar, and that

Answered 11/8

Dr. Joshua Lederberg

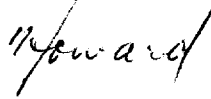
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there would be no error from this source. In any case the experiment should give an accurate comparison of the times of appearance of phenotypic phage resistant, and streptomycin resistant, segregants, and if what I suspect is correct these will differ by from two to three generations.

I shall be extremely glad to have your reactions to the use of the additional mutant locus, and any further details. Again many thanks for having suggested these materials and for your generous offer to attempt to build up stocks.

Sincerely,

A handwritten signature in cursive script, appearing to read "Howard".

Howard B. Newcombe

HBN:ar